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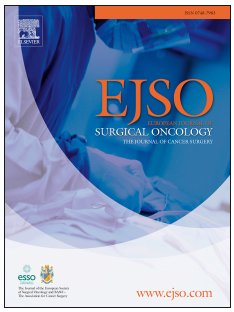

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Poor nutritional status is associated with other geriatric domain impairments and adverse postoperative outcomes in onco-geriatric surgical patients – A multicentre cohort study

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ABSTRACT

Background: Nutritional status (NS), though frequently affected in onco-geriatric patients, is no standard part of a geriatric assessment. The aim of this study was to analyse the association between a preoperatively impaired NS and geriatric domain impairments and adverse postoperative outcomes in onco-geriatric surgical patients.

Methods: 309 patients ≥70 years undergoing surgery for solid tumours were prospectively recruited. Nine screening tools were preoperatively administered as part of a geriatric assessment. NS was based on BMI, weight loss and food intake. Odds ratio's (OR) and 95% confidence intervals (95%CI) were estimated using logistic regression analysis. The occurrence of 30-day adverse postoperative outcomes was recorded.

Results: At a median age of 76 years, 107 patients (34.6%) had an impaired NS. Decreased performance status and depression were associated with an impaired NS, when adjusted for tumour characteristics and comorbidities ($OR_{PS>1}$ 3.46; 95%CI 1.56-7.67. $OR_{GDS>5}$ 2.11; 95%CI 1.05-4.26). An impaired NS was an independent predictor for major complications (OR 3.3; 95%CI 1.6-6.8). Ten out of 11 patients who deceased had an impaired NS.

Conclusion: An impaired NS is prevalent in onco-geriatric patients considered to be fit for surgery. It is associated with decreased performance status and depression. An impaired NS is a predictor for adverse postoperative outcomes. NS should be incorporated in a geriatric assessment.

Keywords: Nutritional status; Geriatric assessment; Surgery; Postoperative complications; Oncology; Aged

INTRODUCTION

Cancer is primarily a disease of the elderly. Currently, 50% of all malignancies are diagnosed in patients 65 years and older and it is predicted this percentage will increase to 70% by 2030[1]. Surgery plays an essential role in the treatment of solid tumours and it is therefore expected that increasing numbers of onco-geriatric patients will require surgery. Whilst fit onco-geriatric patients might recover from surgery as well as their younger counterparts, it is acknowledged that patients with geriatric domain impairments are at an increased risk of adverse postoperative outcomes, mortality and discharge to a non-home institution[2-5]. The preoperative identification of these impairments, utilizing screening elements of a Geriatric Assessment (GA), is essential in this heterogeneous population of onco-geriatric surgical patients.

Though not frequently included in a GA[6], nutritional status (NS) is one of the geriatric domains that is frequently impaired in onco-geriatric patients[7-9]. Recent studies on middle-aged and elderly cancer patients, reported high numbers of patients at nutritional risk or being malnourished (32% to 64.2%)[7-9]. These studies were performed amongst cohorts in which the majority of patients was diagnosed with advanced disease (80.6% stage III/IV and 46.3% with metastases, respectively)[7,9] and frequently underwent chemotherapy with palliative intent (58.3%)[8]. Advanced disease is a known risk factor for malnutrition and many chemotherapeutic treatments are infamous for their side effects, such as nausea, vomiting and mucositis, increasing the risk for malnutrition even further[10,11]. However, in recent *surgical* onco-geriatric cohorts with fewer patients with advanced disease, the prevalence of an impaired NS or risk thereof was also as high as 34.1% and 48%, respectively[12,13].

As nutritional impairment is rather a multifactorial than an isolated problem, improving the understanding of geriatric domain impairments associated with malnourishment could lead to timely preventive measures[14]. For that, the aim of this study was to analyse the association between preoperatively impaired NS, the impairments in other geriatric domains, and the occurrence of adverse postoperative outcomes in onco-geriatric surgical patients.

MATHERIALS AND METHODS

Design and cohort definition

Data were derived from the preoperative risk estimation for onco-geriatric patients (PREOP) study, an international prospective cohort study. The PREOP-study was approved by the appropriate ethics committees and was registered at the Dutch Trial register (Trial ID: NTR1567) and United Kingdom register (Research Ethics Committee reference: 10/H1008/59).

Data deriving from centres that included less than ten patients were excluded from analyses, to reduce the influence of selection bias. Of the 14 medical centres initially adhering to the project, eight were able to enrol ten or more patients in the present study. When peri- or postoperatively patients appeared to have a benign condition (n=19), they were excluded from further analyses as the association between cancer and NS is an important factor in the current analyses.

The detailed cohort definition and study protocol were published previously[12,15]. In summary, patients aged 70 years and older, undergoing elective surgery for a solid tumour were included. Preoperatively, a battery of screening tools, assessing all domains recommended for a GA, was administered (Table 1). Screening tools that assessed multiple geriatric domains were excluded from analyses, as these will not provide an answer to the research question of the current study. Complications up to 30 days after surgery were registered using the Clavien-Dindo classification. Major complications were defined as grade three to grade five, which were complications requiring surgical, endoscopic or radiological intervention (grade 3); life threatening complications requiring intensive care management (grade 4); and death of a patient (grade 5)[26].

Nutritional status

To determine the risk for an impaired NS, the nutritional risk screening (NRS) scale, based on the NRS-2002, was used[24]. Patients were stratified according to the following criteria:

- Normal NS

- Mildly impaired NS: weight loss greater than 5% in the previous three months or a food intake below 50-75% of normal requirement in the preceding week;
- Moderately impaired NS: weight loss greater than 5% in the previous two months or a body mass index (BMI) between 18.5 and 20.5 kg/m^2 and impaired general condition or a food intake below 25-50% of normal requirement in the preceding week;
- Severely impaired NS: weight loss greater than 5% in the previous month or a weight loss greater than 15% in three months or a BMI less than 18.5 kg/m^2 and an impaired general condition or a food intake below 25% of normal requirement in the preceding week.

Statistical analysis

Results on the geriatric screening tools and the occurrence of major postoperative complications were analysed as dichotomized values, based on predefined, literature based cut-off points. Categorical data were described as frequencies and proportions, and continuous variables as median and interquartile range (i.q.r.). For further analyses, NS was considered as a dependent variable. Logistic regression analysis was used to estimate odds ratio's (OR) and 95% confidence intervals (95% CI), which were at least adjusted for centre. Both complete cohort analyses as well as a sub-group analyses for patients with intra-abdominal tumours were performed. Firstly, the associations between patients' demographics and disease characteristics and NS (impaired versus normal) were estimated. Subsequently, the associations between the geriatric screening tools and NS were estimated in a model adjusted for centre (model 1) and in a model adjusted for statistically significant confounders (model 2 for the complete cohort or model 3 for patients with intra-abdominal tumours).

The association between an impaired NS and other geriatric domain impairments as independent variables and the occurrence of major postoperative complications as a dependent variable, was estimated using backwards stepwise logistic regression analysis, whilst forcing statistically significant patients' and disease characteristics into the model[12]. The association between an impaired NS and 30-day mortality was evaluated using Fisher's exact test.

Missing values for the geriatric screening tools were addressed by multiple imputation, as the missing values were supposed to be missing (completely) at random. Multiple imputation was performed for the total scores on the questionnaires and was based on available results on the screening tools, age, gender, living situation, preoperative haemoglobin level, type of tumour, tumour stage, type of surgery and number of comorbidities[12,27]. The reported results on the screening tools were pooled values, which were average values calculated from the five imputed datasets[12].

Missing values for tumour stage (n=32) were not addressed by multiple imputation, leading to multivariate logistic regression analyses of 277 cases for model 2. Sensitivity analyses were performed for model 1, to discover possible discrepancies between complete case analyses based on model 2 and analyses of the entire cohort.

Data analysis and multiple imputation were performed using IBM SPSS Statistics 23. P-values ≤ 0.05 were considered statistically significant.

RESULTS

Baseline characteristics

Data of 309 patients deriving from eight medical centres were analysed. Baseline characteristics are shown in table 2. A total of 190 patients were female (61.5%) and the median age was 76 years (i.q.r.: 8). The vast majority of patients had an intra-abdominal tumour (n = 207; 67%). Patients were most frequently planned for colorectal and breast cancer surgery (n=117, 37.6% and n=77, 24.8%, respectively). The 9 tumour sites that were classified as remaining, were thyroid (n=5), anus (n=3) and prostate (n=1). The pathologists' reports confirmed stage 1, 2, 3 and 4 disease in 76 (24.6%), 83 (26.9%), 65 (21%) and 53 (17.2%) patients, respectively.

Nutritional status

Table 3 shows the associations between the patients' demographics and disease characteristics and NS. A total of 202 (65.4%) patients were defined as having a normal NS, 81 (26.2%) had a mild nutritional impairment and 26 (8.4 %) had a moderate or severe nutritional impairment. Advanced age was overall not statistically significantly associated with the risk for an impaired NS, except for the group aged 80 to 84 years old (OR 2.2; 95% CI 1.1-4.5). A high number of comorbidities was associated with an impaired NS (OR 2.10; 95% CI 1.20-3.68). Patients with a tumour located in the pancreas, biliary tract, stomach, oesophagus, kidney, bladder, colon or rectum had the highest risks for an impaired NS. With increasing tumour stage, the risk for an impaired NS increased as well, whilst the 95% CI's did overlap (Stage 3: OR 2.1; 95% CI 1.1-3.9. Stage 4: OR 2.6; 95% CI 1.2-5.4). In a sub-group analysis on patients with intra-abdominal tumours, a high number of comorbidities and a tumour located in the pancreas or biliary tract were associated with an impaired NS ($OR_{Comorbidities \geq 4}$ 2.4; 95% CI 1.3-4.5. $OR_{pancreas\ and\ biliary\ tract}$ 3.1; 95% CI 1.1-8.4 with reference to colorectal cancer).

Geriatric domains associated with nutritional status

A total of 65.4% of the patients with an ECOG PS >1 had an impaired NS (Table 4). Furthermore, an impaired functional status or signs of depression were frequently accompanied by an impaired NS (51.9% of $TUG_{>20}$, 50.7% of $ADL_{>0}$ and 50.6% of $GDS_{>5}$). The majority of patients that did not have a geriatric domain impairment, had a normal NS as well (ranging from 68.9% for $TUG_{\leq 20}$ to 73.7% for $IADL_{8}$). The domains significantly associated with an impaired NS were ECOG PS ($OR_{PS>1}$ 3.5; 95% CI 1.6-7.7) and GDS ($OR_{GDS>5}$ 2.1; 95% CI 1.1-4.3), when adjusted for centre, age, comorbidities, tumour site and tumour stage (Table 4, model 2). In a sub-group analysis on patients with intra-abdominal tumours ADL ($OR_{ADL>0}$ 2.2; 95% CI 1.1-4.6), IADL ($OR_{<8}$ 2.8; 95% CI 1.5-5.5), ECOG PS ($OR_{ECOG\ PS>1}$ 3.4; 95% CI 1.4-8.0) and GDS ($OR_{GDS>5}$ 2.3; 95% CI 1.1-4.8) were significantly associated with an impaired NS, when adjusted for centre and comorbidities (Table 4, model 3).

Nutritional status and adverse postoperative outcomes

A total of 160 (51.8%) patients experienced at least one complication within 30 days after surgery. Major complications occurred in 57 (18.4%) patients, including death in 11 patients (30-day mortality rate: 3.6%). Of the 11 patients who deceased within 30 days postoperatively, ten patients had an impaired NS (90.9%) ($p<0.001$). Of all patients with a normal NS, 90.6% did not experience any major postoperative complications. Of all patients with an impaired NS, 35.5% experienced major postoperative complications. The best combination of screening tools with regard to predicting the risk for major postoperative complications comprised an assessment of NS, TUG and ASA score (table 5), as was previously shown[12]. We therefore reinforce the statement that the assessment of NS preoperatively, allows a clear understanding of the operative risk.

DISCUSSION

Onco-geriatric patients undergoing elective surgery, can be considered a selected and thus relatively fit part of the onco-geriatric population[28]. Nevertheless, an impaired NS was frequently seen in this cohort of onco-geriatric surgical patients (34.6%). An impaired NS was associated with both tumour characteristics and an increased number of other comorbidities as well as decreased performance status, signs of depression and an impaired functional status. An impaired NS is an important predictor for major complications including death.

The prevalence of an impaired NS is comparable with several other cohorts of onco-geriatric patients, whilst a lower prevalence was to be expected as fewer patients (38.2%) were diagnosed with advanced disease[7-9]. This discrepancy between observed and expected values can be explained by either an underestimation of the prevalence of malnutrition in the other cohorts, an overestimation in the current study or by the fact that the other cohorts concern selected patients as well, i.e. with no or few geriatric domain impairments. Bozzetti et al. assessed NS using the NRS-2002, which is similar to the nutritional screening in the current study and has proven to be suitable for use in hospitalized patients and, specifically, in cancer patients[7,29]. The study by Aaldriks et al. administered the Mini Nutritional Assessment, which has been validated for elderly people, with a sensitivity of 96% and specificity of 98% in elderly patients (not specifically cancer patients), and was found to be able to detect a risk of malnutrition before changes in weight or albumin levels occurred[8,30]. Thus underestimation of the prevalence of malnutrition in the other studies or an overestimation in the current study are unlikely.

It is likely that these cohorts of patients, undergoing active anti-cancer treatment or at least able to attend an ambulatory consultation, consist of selected and relatively fit patients as well. This hypothesis is substantiated by the higher prevalence of (risk of) malnutrition in another study of onco-geriatric patients by Paillaud et al. (64.2%)[9]. Participants of this study were patients that were referred to a geriatric oncology clinic, thus with a higher a priori chance of geriatric domain impairments. This was subsequently confirmed

by, for example, a $PS_{>1}$ in 50.4% of patients, compared to 16.8% in the current cohort and 20% in the cohort from Bozzetti et al., and a $MMSE_{\leq 24}$ in 29.8%, compared to 9% in the cohort from Aaldriks et al. These results suggest that, maybe even stronger than disease characteristics, geriatric domain impairments are associated with NS. It should be emphasized that these prevalences of an impaired NS stem from cohorts in which a decision on treatment modality had already been made and thus, extrapolating results to all onco-geriatric patients in daily clinical practice should occur with caution.

The results of the current study show that in onco-geriatric patients, independent of tumour site and stage and comorbidities, impairments in the geriatric domains performance status, mood and functional status are associated with the risk of an impaired NS. The results maintained in a sub-group analysis on patients with intra-abdominal tumours, whom are at greatest risk for both an impaired NS[7,9] and adverse outcomes after major surgery[12]. The results are comparable to results found in different studies including onco-geriatric patients or elderly hospitalized patients[9,31-33]. Other associated geriatric domain impairments were cognitive and mobility impairments, which were assessed with the MMSE, TUG and risk of falls.

The importance of preoperative nutritional screening is emphasized by the fact that out of all geriatric screening tools, an impaired NS – combined with TUG-score and ASA status – was best in predicting the occurrence of major postoperative complications. On top of that, ten out of 11 patients who deceased within 30-days postoperatively, had an impaired NS. Similarly, in patients ≥65 years undergoing pancreaticoduodenectomy for benign disease, a ‘Severe Nutritional Risk’ was found to be a prognostic factor for long-term survival (adjusted hazard ratio 2.74; 95% CI 1.25-6.02)[34]. Furthermore, NS, assessed either by the MNA-score, recent weight loss, body mass index (BMI) or serum albumin levels, are known prognostic factors of survival and response to chemotherapy in cancer patients[5,8,35]. Data on the predictive ability of nutritional markers on postoperative outcomes in the elderly general surgery and hip surgery patient populations are scarce and nutritional markers are operationalized in several ways, according to a systematic review including 15 studies[36]. Serum albumin is a frequently investigated nutritional

parameter (13 out of 15 studies) with – overall – positive results regarding its predictive ability of postoperative outcomes such as postoperative complications, mortality and length of hospital stay. However, serum albumin might be merely a marker of inflammatory metabolism rather than a pure representative of nutritional status in surgical patients[36]. Three included studies used a nutritional questionnaire, such as the MNA or the food frequency questionnaire. These were not associated with adverse postoperative outcomes. Out of 15 studies, one was comparable to the current study: a retrospective study on elderly gastrointestinal surgery patients, which found ≥10% weight loss in 6 months as a risk factor for postoperative morbidity. Despite promising results regarding weight loss, BMI and serum albumin levels, based on the current literature it can be concluded, that no consensus has been reached as to what an appropriate nutritional screening tool entails and what its' exact value is.

The use of nutritional interventions in order to improve these outcomes has not been clearly established yet[35,37,38]. A meta-analysis on the influence of nutritional support on adverse outcomes in cancer patients, showed no advantage for the intervention arms[37]. It was noted that the lack of effect might be attributed to poor study designs and heterogeneous patient populations. However, colorectal cancer patients subjected to a so-called trimodal prehabilitation program, consisting of nutritional counselling, protein supplementation, anxiety reduction exercises and physical exercise, showed improved functional outcome after surgery[39]. Furthermore, over the last several years, multiple studies suggested that enhanced recovery programs for elderly surgical patients were feasible and led to equally positive results as compared to their younger counterparts[40-42]. Unfortunately, elderly patients have high variability within their own group and what was demonstrated for patients with colorectal cancer, was not repeated for elderly patients with gastric cancer[43]. These results endorse the importance of an integrated approach in cancer patients, assessing at least NS, performance status and mood. Furthermore, more than from a strict list of postoperative prescriptions within a protocol, selected elderly patients might benefit from controlled and tailored (p)rehabilitation programmes.

Due to the cross-sectional nature of the current analyses, no clear conclusions on possible causal relations regarding NS and impairments in other geriatric domains can be drawn. The association between an impaired NS, functional status and depression can go both ways and the influence of common risk factors, such as disease burden and social factors, cannot be ignored.

It can be hypothesized that the link between impaired NS, depression, functional impairment and adverse postoperative outcomes, is via inflammatory pathways. It is known that aging is accompanied by a low-grade inflammatory state and that increased levels of pro-inflammatory cytokines are associated with functional decline, multiple geriatric domain impairments, frailty and mortality in the elderly[44-46]. Furthermore, cancer patients, especially in an advanced stage, are at risk for cachexia. This is a complex and systemic syndrome characterized by loss of skeletal muscle mass (with or without loss of fat mass), often accompanied by reduced food intake and systemic inflammation and frequently leading to functional impairment[47]. Finally, bidirectional associations between diet and depression via inflammatory pathways, have been postulated. Diet can either promote or attenuate inflammatory effects, inflammation can induce 'sickness behaviour' including depressive symptoms in susceptible persons and depression can increase pro-inflammatory cytokine production[48,49]. On top of that, depressed patients elicit higher inflammatory responses to physical and psychological stress[49], thus putting them at increased risk for adverse outcomes after a major stressor such as surgery. Future research should point out whether these hypotheses can be confirmed in an onco-geriatric population, in which multiple parameters (e.g. aging, tumour biology and cancer treatment effects) influence the inflammatory state[50].

The main strength of our study is its comprehensive and detailed assessment of patients' demographics, disease characteristics and geriatric domains in a cohort of onco-geriatric surgical patients, who were prospectively recruited in multiple centres from different countries. Previous studies have focused on impaired NS and its association with other geriatric domain impairments in cohorts including many *non*-surgical patients with advanced disease and/or undergoing palliative treatment, whereas the current study

focused on patients that were considered fit for surgery and were, moreover, less frequently diagnosed with advanced disease. These results should raise awareness amongst surgeons on NS being a multifactorial and prevalent issue in their patient population.

An impaired NS is frequently seen in onco-geriatric patients considered to be fit for surgery. The results of the current study confirm that an impaired NS is associated with functional impairments and possible depression in these patients. Moreover, our data substantiate that NS is an important risk factor for adverse postoperative outcomes. This emphasizes the importance of a geriatric assessment in onco-geriatric surgical patients and that a nutritional assessment should be an essential part of this. Identification of the patients with an impaired NS is of the utmost importance, especially as they might benefit from preventive strategies.

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Conflict of interest

All authors have no conflicts of interest to declare.

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Table 1. Components of PREOP

Test	Acronym	Purpose	Cut-off value for adverse results	Range of possible scores
Timed Up and Go[16] [a]	TUG	a walking test to measure functional status	>20 seconds[b]	Not applicable
Activities of Daily Living[17]	ADL	depicts dependency regarding bathing, dressing, toileting, transfer, continence and feeding	>0	0 - 12
Instrumental Activities of Daily Living[18]	IADL	a questionnaire regarding 8 items needed to perform independently to maintain independence in the community	<8	0 - 8
Eastern Cooperative Oncology Group performance status[19]	ECOG PS	a physician's perspective of a patient's functional status; ranging from 0 to 4	>1	0 - 4
Mini Mental State Examination[20]	MMSE	a test consisting of 11 questions to assess cognitive function	≤26	0 - 30
Geriatric Depression Scale[21]	GDS	a 15-item self-rating depression screening scale for elderly populations	>5	0 - 15
Brief Fatigue Inventory[22]	BFI	a 9-item questionnaire to report on fatigue severity in cancer patients	>3	0 - 10

American Society for Anaesthesiologist scale[23][c]	ASA	to quantify preoperative physical status and estimate anaesthetic risk	≥3	1 - 5
Nutritional Risk Screening[24]	NS	nutritional status based on recent weight loss, overall condition and reduction of food intake	Impaired nutritional status was compared to normal nutritional status	Normal to severely impaired nutritional status

[a] Patients performed the TUG two times and for each patient, the mean of the two time measurements was calculated; [b] based on literature and the distribution of the mean values in the current study population, a score of less than or equal to 20 seconds on the TUG was considered a low score[25]; [c] the ASA-classification was determined by an anaesthesiologist.

Table 2. Patients' characteristics	
Variable	**Value**
Gender, female	190 (61.5)
Age	
70-74	110 (35.6)
75-79	99 (32.0)
80-84	69 (22.3)
≥85	31 (10.0)
Weight (kg)[a]	
Female	67 (15.6)
Male	73 (14.6)
BMI (kg/m^2)[a]	
Female	26 (5.8)
Male	25 (3.9)
Living situation	
Independent/family	304 (99.3)
Residential care/nursing home	2 (0.7)
Comorbidities[a]	3 (2)

Cancer site[b]	
Superficial	102 (33.0)
Intra-abdominal	207 (67.0)
Breast	77 (24.8)
Colorectal	117 (37.6)
Gastric and oesophageal	22 (7.1)
Gynaecological	18 (5.8)
Pancreas and biliary tract	29 (9.3)
Remaining	9 (2.9)
Renal and bladder	23 (7.4)
Soft tissue and skin	16 (5.1)
Tumour stage	
Stage 1	76 (24.6)
Stage 2	83 (26.9)
Stage 3	65 (21.0)
Stage 4	53 (17.2)
Unclassified/missing	32 (10.4)

Values in parentheses are percentages unless indicated otherwise; [a] values are median (i.q.r.); [b] one patient was operated on colon and renal cancer and one on melanoma skin cancer and breast cancer: for tumour staging and subsequent analyses the most severe disease was analysed; kg = kilograms; BMI = Body Mass Index

Table 3. Association between patients' characteristics and impaired nutritional status

Variable	Normal nutritional status	Impaired nutritional status	Adjusted OR[b, c]	Adjusted OR[b, d]
Gender				
Female	129 (67.9)	61 (32.1)	1	1
Male	73 (61.3)	46 (38.7)	1.14 (0.67-1.96)	0.74 (0.42-1.33)
Age				
70-74	80 (72.7)	30 (27.3)	1	1
75-79	64 (64.6)	35 (35.4)	1.27 (0.67-2.42)	1.48 (0.71-3.07)
80-84	41 (59.4)	28 (40.6)	**2.22 (1.10-4.48)**	1.97 (0.88-4.41)
≥85	18 (58.1)	13 (41.9)	2.29 (0.93-5.63)	3.13 (0.98-9.99)
Weight (kg)				
Female	68.1 (11.6)[a]	60.0 (19.1)[a]	**0.94 (0.91-0.97)**	**0.95 (0.92-0.99)**
Male	75.2 (12.1)[a]	70.4 (15.8)[a]	**0.94 (0.90-0.99)**	**0.93 (0.89-0.98)**
BMI(kg/m^2)				
Female	26.5 (5.3)[a]	23.6 (6.0)[a]	**0.85 (0.78-0.93)**	**0.90 (0.81-0.99)**
Male	25.4 (3.5)[a]	24.1 (5.2)[a]	**0.82 (0.71-0.96)**	**0.79 (0.67-0.93)**
Comorbidities				
<4	138 (70.1)	59 (29.9)	1	1
≥4	64 (57.1)	48 (42.9)	**2.10 (1.20-3.68)**	**2.39 (1.26-4.54)**
Tumour site				
Superficial	87 (85.3)	15 (14.7)	1	Not applicable
Intra-abdominal	115 (55.6)	92 (4.4)	**3.87 (1.98-7.57)**	

Breast	67 (88.2)	9 (11.8)	1	
Colorectal	72 (61.5)	45 (38.5)	**4.09 (1.74-9.59)**	1
Gastric and Oesophageal	10 (45.5)	12 (54.5)	**9.60 (2.96-31.13)**	2.33 (0.86-6.35)
Gynaecological	15 (83.3)	3 (16.7)	1.18 (0.24-5.81)	0.32 (0.06-1.75)
Pancreas and biliary tract	11 (37.9)	18 (62.1)	**12.27 (3.42-44.03)**	**3.07 (1.12-8.40)**
Remaining	3 (33.3)	6 (66.7)	**11.56 (2.02-66.21)**	4.37 (0.41-47.06)
Renal and bladder	12 (54.5)	10 (45.5)	**7.09 (1.86-27.09)**	1.65 (0.55-4.91)
Soft tissue and skin	13 (81.3)	3 (18.8)	1.76 (0.27-11.45)	Not performed[e]
Tumour stage				
Stage 1 or 2	120 (75.5)	39 (24.5)	1	1
Stage 3	37 (56.9)	28 (43.1)	**2.05 (1.07-3.92)**	1.56 (0.73-3.37)
Stage 4	25 (47.2)	28 (52.8)	**2.58 (1.24-5.37)**	1.76 (0.81-3.83)

Values in parentheses in the second and third column are percentages unless indicated otherwise; values in parentheses in the final two columns are 95% CI; [a] values are median (i.q.r.); [b] adjusted for centre; [c] analysis of complete cohort; [d] sub-group analysis of patients with intra-abdominal tumours; [e] only one patient with an intra-abdominal soft tissue tumour; kg = kilograms; BMI = Body Mass Index; **Bold** = statistically significant (≤ 0.05)

Table 4. Association between geriatric screening tools and impaired nutritional status

Geriatric screening tool[a]	Normal nutritional status	Impaired nutritional status	Adjusted OR model 1[b, d]	Adjusted OR model 1[c, d]	Adjusted OR model 2[b]	Adjusted OR model 3[c]
TUG						
≤20 s	177 (68.9)	80 (31.1)	1	1	1	1
>20 s	25 (48.1)	27 (51.9)	1.99 (0.89-4.49)	1.42 (0.53-3.78)	1.12 (0.41-3.09)	1.14 (0.41-3.18)
ADL						
0	168 (70.6)	70 (29.4)	1	1	1	1
>0	35 (49.3)	36 (50.7)	**2.16 (1.17-3.99)**	**2.41 (1.17-4.95)**	1.66 (0.84-3.28)	**2.23 (1.07-4.63)**
IADL						
8	137 (73.7)	49 (26.3)	1	1	1	**1**
<8	66 (53.7)	57 (46.3)	**2.20 (1.29-3.75)**	**3.11 (1.63-5.92)**	1.67 (0.88-3.16)	**2.82 (1.46-5.45)**
ECOG PS						
≤1	184 (71.6)	73 (28.4)	1	1	1	1
>1	18 (34.6)	34 (65.4)	**4.41 (2.16-8.97)**	**3.68 (1.60-8.48)**	**3.46 (1.56-7.67)**	**3.38 (1.44-7.95)**

MMSE						
>26	135 (70.3)	57 (29.7)	1	1	1	1
≤26	67 (57.3)	50 (42.7)	1.66 (0.98-2.80)	1.72 (0.93-3.16)	1.33 (0.72-2.45)	1.56 (0.84-2.91)
GDS						
≤5	160 (71.4)	64 (28.6)	1	1	1	1
>5	42 (49.4)	43 (50.6)	**2.32 (1.25-4.30)**	**2.43 (1.16-5.10)**	**2.11 (1.05-4.26)**	**2.25 (1.06-4.77)**
BFI						
≤3	128 (69.2)	57 (30.8)	1	1	1	1
>3	74 (59.7)	50 (40.3)	1.49 (0.87-2.56)	1.56 (0.83-2.93)	1.13 (0.61-2.12)	1.39 (0.73-2.66)
ASA-score						
<3	124 (71.7)	49 (28.3)	1	1	1	1
≥3	78 (57.4)	58 (42.6)	**2.39 (1.39-4.12)**	**2.14 (1.13-4.04)**	1.56 (0.81-2.99)	1.69 (0.86-3.35)

Values in parentheses in the second and third column are percentages; values in parentheses in the other columns are 95% CI; [a] acronyms of the screening tools are spelled out in table 1; model 1 is adjusted for centre.; model 2 is adjusted for centre, age (continuous), comorbidities (<4 or ≥4), tumour site (intra-abdominal versus superficial) and tumour stage (1-4); model 3 is adjusted for centre and comorbidities (<4 or ≥4); [b] analysis of complete cohort; [c] sub-group analysis of patients with intra-abdominal tumours; [d] sensitivity analyses were performed for model 1 with the complete cases of model 2 (minus 32 cases in which tumour stage was missing): n=277 for complete cohort and n=179 for sub-group

analysis: similar results were found **(**data not shown); **Bold** = statistically significant (≤ 0.05)

Table 5. Association between geriatric screening tools and major postoperative complications	
Geriatric screening tool[a]	**Adjusted OR[b]**
NS	
Normal	1
Impaired	3.3 (1.6-6.8)
TUG	
≤20 s	1
>20 s	3.1 (1.1-8.6)
ASA-score	
<3	1
≥3	2.8 (1.2-6.3)
Values in parentheses are 95% CI; [a]acronyms of the screening tools are spelled out in table 1; [b]adjusted for centre, gender and type of surgery	